IN THE CLAIMS

Please amend the claims as follows:

1. (Previously presented) A method for producing isolated galactose oxidase comprising transforming a yeast with a vector comprising a nucleic acid sequence encoding a fusion protein of a signal peptide and galactose oxidase, and an inducible promoter that regulates transcription of the sequence encoding said fusion protein, culturing said transformed yeast at a first temperature, inducing said promoter at a second temperature which is lower than the first temperature to cause yeast to produce said fusion protein, removing within the yeast said signal peptide from the galactose oxidase, and secreting the galactose oxidase from the yeast, wherein the galactose oxidase is in an inactive form when secreted from the yeast.

2. (Original) The method of claim 1 which further comprises activating the secreted galactose oxidase by treatment with an oxidant.

3. (Original) The method of claim 1 wherein the yeast is *Pichia spp.*

4. (Previously presented) The method of claim 1 wherein the signal peptide is an *Aspergillus niger* glucoamylase signal peptide.

5. (Original) The method of claim 1 wherein the inducible promoter is a methanol-inducible promoter.

6 to 17. (Canceled)

18. (Previously presented) The method of claim 1 wherein the temperature during the induction is 25°C.

19. (Canceled)

20. (Previously presented) A method for producing isolated galactose oxidase comprising transforming a yeast with a vector comprising a nucleic acid sequence encoding a fusion protein of a signal peptide and galactose oxidase, and an inducible promoter that regulates transcription of the sequence encoding said fusion protein, culturing said transformed yeast, inducing said promoter to cause yeast to produce said fusion protein, removing within the yeast said signal peptide from the galactose oxidase, secreting the galactose oxidase from the yeast, wherein the galactose oxidase is in an inactive form when secreted from the yeast, and activating the secreted galactose oxidase by treatment with an oxidant for12 hours.

21. (Currently amended) The method of claim 20 wherein the culturing is at a first temperature and the inducing is at a second temperature which is lower than the [first] temperature <u>of culturing</u>.

22. (Previously presented) The method of claim 21 wherein the second temperature is 25°C.

REMARKS

Applicants submit this Amendment in response to the Office Action of August 22, 2003. Applicants note that the present Office Action is not a final rejection.

Claim 21 has been amended for clarification.

The Examiner stated, on page 2 of the Office Action, that claims 1-5, 18, and 20-21 are pending. Applicants respectfully note that claims 1-5, 18, and 20-22 are pending in the application.

Rejections of the Claims

I. Rejection of claims 1, 3-5, and 18 under 35 U.S.C. §103(a)

A. The Examiner has rejected claims 1, 3-5, and 18 under 35 U.S.C. §103(a) as being unpatentable under 35 U.S.C. §103(a) over the combined disclosure of Golightly in view of Zamost. The Examiner has further relied upon McAleer, Virus Genes, 20(2):127-133 (2000) to support this basis of rejection. Applicants traverse the rejection of these claims on this ground.

In response to the previous Office Action, mailed on April 22, 2003, Applicants amended independent claim 1 to incorporate features in the dependent claims that were not rejected over the prior art. In the present Office Action, the Examiner has not rejected the claims that contain these features and relies, in order to support this rejection, on prior art that was published either after the priority date of the present application or after the date which is one year prior to the date of priority date of the present application.

The Examiner has framed the rejection as being over Golightly and Zamost and has cited McAleer in order to show obviousness. However, Applicants submit that the present rejection in

truth relies upon the disclosure of McAleer, which discloses a novel aspect not previously disclosed in the prior art.

As disclosed in McAleer (see the Abstract):

> The effects of culture volume, temperature, and methanol concentration on the levels of expression, were studied. The results indicate that there is a balance required between the induction temperature and methanol concentration to achieve maximal expression.

The Examiner asserts that this disclosure provides support for the rejection for obviousness over Golightly and Zamost.

Applicants respectfully submit that the rejection on this ground is improper. Applicants submit that the present rejection is, in fact, a rejection over the combined disclosures of Golightly, Zamost, and McAleer and that such a basis for rejection is improper because McAleer is not citable prior art against the present application. Thus, the Examiner is requested to reconsider and withdraw the rejection of the claims on this ground.

Applicants further submit that the McAleer reference, rather than providing an indication that the present invention is obvious, establishes the unobviousness of the present invention. The McAleer article discloses a study that was performed to determine the effect of induction temperature upon the level of expression in *Pichia*. Prior to the McAleer article, the effect of induction temperature on the *Pichia* system was unknown. Rather than indicate that such a step is obvious, the fact that the McAleer study was performed and published to establish this effect indicates that the lower temperature for induction is not obvious.

The present inventors have discovered this previously unknown property of induction temperature and found, unexpectedly, that protein yields are increased. The present invention is

a method for producing a particular protein, which method calls for the novel step of lowering the temperature during induction. The prior art that is applicable to the present invention, that is Golightly and Zamost without McAleer, does not disclose or suggest the invention called for in the claims. Accordingly, Applicants submit that the present invention, as called for in claims 1, 3-5, and 18 patentably distinguishes over the prior art and the Examiner is requested to reconsider and to withdraw the rejection of these claims on this ground.

B. The Examiner has rejected claims 1, 2, and 20-22, under 35 U.S.C. §103(a) as being unpatentable under 35 U.S.C. §103(a) over the combined disclosure of Golightly in view of Zamost and Montague. The Examiner has stated that the Golightly and Zamost references are applied as to claims 1, 3-5, and 18 above. The Golightly and Zamost references were applied to the rejection of claims 1, 3-5, and 18 with additional reliance upon McAleer, Virus Genes, 20(2):127-133 (2000) to support this basis of rejection. Applicants traverse the rejection of these claims on this ground.

Applicants submit that claims 1 and 2 are patentable over the prior art for the reasons stated above in Section A in the discussion of the rejection of claims 1, 3-5, and 18 over Zamost and Golightly (and McAleer).

Claim 20 is an independent claim and claims 21 and 22 depend therefrom. These claims call for a prolonged treatment with an oxidant (12 hours). Moreover, claims 21 and 22 call for a temperature of induction which is lower than the temperature of culturing. Applicants submit that these claims are patentable for the same reason that claims 1-5, and 18 are patentable, as discussed above.

Moreover, Applicants submit that the feature of prolonged treatment with an oxidant of claims 20 to 22 further establishes patentability of these claims.

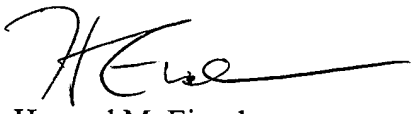
Montague-Smith discloses treatment with an oxidizing agent for a brief period of time, about 15 minutes (see page 354, column 1, last line and Table 1). The present claims call for a 12 hour treatment. Such prolonged treatment prevents the degradation of the active form of galactose oxidase to an inactive form, which occurs following the procedure of Montague-Smith due to the presence of contaminants associated with the protein. The Applicants have discovered that prolonged oxidation, not disclosed or suggested by Montague-Smith, results in stable active galactose oxidase, such as is not produced by the method of Montague-Smith.

Applicants submit that the prior art does not disclose or suggest the invention called for in claims 1, 2, or 20-22. Accordingly, Applicants respectfully request the Examiner to reconsider and to withdraw the rejection of these claims on this ground.

CONCLUSION

Applicants submit that the present claims are in condition for allowance and request an early notification to that effect.

Respectfully submitted,



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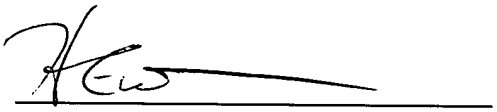
CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on October 27, 2003.

Dated: 10/27/03



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